REMARKS

Claims 37-62 are pending in the instant application. Claims 37-62 have been rejected. Claims 37, 50 and 61-62 have been amended. Claims 42-45, 47 and 48 have been canceled. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Withdrawn Objections/Rejections

Applicants acknowledge the withdrawal of the objections of the specification and claims, the rejection of claims 1-4 under 35 U.S.C. 102(b) as being anticipated by Neri et al. (US 4,474,813), the rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Neri et al. (US 3,995,060), and the rejection of claims 2-4 under 35 U.S.C. 103(a) as being unpatentable over Neri et al. (US 3,995,060).

II. Claim Objections

Claims 39 and 61-62 have been objected to. It is suggested that "mixer" is misspelled as "mixture" in these claims. Applicants note that the term "mixture" does not appear in claim 39, but rather is present in claim 37. Thus, Applicants have made the appropriate amendments to claims 37 and 61-21 and respectfully request that this objection be withdrawn.

III. Rejection of the Claims Under 35 U.S.C. §112

Claim 42 has been rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. It is suggested that the limitation "…

wherein the flutamide particles comprise a mean particle size greater than the mean particle size of flutamide that, with an initial particle size of from 5 to 240 μm, has been subjected to a milling operation," is unclear. Applicants respectfully disagree. However, in the interest of facilitating the prosecution of this application, Applicants have canceled claim 42. It is therefore respectfully requested that this rejection be withdrawn.

Claim 50 has been rejected under 35 U.S.C. 112, first paragraph, for failing to meet the enablement requirement. It is suggested that while the specification is enabling for the free acid amide of flutamide, the specification does not enable pharmaceutically acceptable solvates of flutamide. Applicants respectfully disagree. However, claim 50 has been amended to remove reference to pharmaceutically acceptable solvates of flutamide to facilitate the prosecution of this application. It is therefore respectfully requested that this rejection be withdrawn.

IV. Rejection of the Claims Under 35 U.S.C. §102

Claims 37-40, 42-43, 47-48, and 50-62 have been rejected under 35 U.S.C. 102(b) as being anticipated by James et al. (U.S. Patent No. 6,228,401). It is suggested that the instant claims are product-by-process claims and the patentability of a product does not depend on its method of production. It is suggested that James et al. teach flutamide mixed with at least one surface-active substance, *e.g.*, sodium lauryl sulfate. The Examiner acknowledges that James et al. do not explicitly state that the flutamide is crystalline and/or amorphous; however, because there

are no other known forms of flutamide, the flutamide of James et al. must be crystalline and/or amorphous. The Examiner asserts that James et al. teach rotary cutters as one means of achieving the desired flutamide particle size, wherein rotary cutters are a type of force-action mixer. It is further suggested that James et al. teach the various embodiments set forth in instant claims 38-40, 42-43, 47-48, and 50-62 thereby anticipating the same.

Applicants respectfully disagree with this rejection. At the outset, Applicants respectfully submit that while claims 61-62 have been included in this rejection, the Examiner has not cited any teachings of James et al. that relate to the subject matter of these claims. As Applicants pointed out at page 11 of the Reply dated November 6, 2008, a composition containing unmilled flutamide, which has been subjected to intensive mixing (*e.g.*, for 1 to 180 minutes) with a forced-action mixer in the presence of at least one surface-active substance, exhibits not only reproducible, but also higher rates of release of flutamide than formulations including micronised flutamide. Thus, such intensive mixing imparts a distinct size and structure to the claimed composition which facilitates release.

MPEP §2113 instructs that "[t]he structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. [citing *In re Garnero*, 162 USPQ 221,223 (CCPA 1979]."

Accordingly, in an earnest effort to highlight the distinct size of the particles of the instant composition, Applicant has amended claim 37 to specify that the size of 50% of the flutamide particles is greater than 26 μm. Support for this amendment is found in claim 44. Therefore, claim 44 has been canceled. In addition, claim 43 has been canceled as it no longer further limits claim 37 as amended.

Anticipation is established only when a single prior art reference discloses, expressly or under the principles of inherency, each and every element of a claimed invention. *RCA Corp. v. Applied Digital Data Sys., Inc.*, 730 F.2d 1440, 1444 (Fed. Cir. 1984).

In so far as James et al. fail to teach or suggest the pharmaceutical formulation as currently presented, this reference cannot be held to anticipate the present invention. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

V. Rejection of the Claims Under 35 U.S.C. §103

Claims 44-46 and 49 have been rejected under 35 U.S.C. 103(a) as being unpatentable over James et al. (U.S. 6,228,401). It is suggested that James et al. teach that the specific surface area and particle size of flutamide influence bioavailability of flutamide and that James et al. teach milling and rotary cutters for achieving appropriate particle sizes, distributions and surface areas. It is suggested that one of skill in the art would be motivated to alter the particular size distribution and surface area of particles in order to arrive at a set of flutamide particles with optimal bioavailability.

Claim 41 has also been rejected under 35 U.S.C. 103(a) as being unpatentable over James et al. in further view of Neri et al. (US 3,995,060). It is suggested that while James et al. fail to teach that flutamide has been subjected to recrystallisation as necessitated by claim 41, Neri et al. compensate for this deficiency in the teachings of the primary reference.

Applicants respectfully traverse these rejections. As asserted by the Examiner at page 13 of the Office Action, James et al. teach the relative insolubility of flutamide; the influence of surface area of flutamide on bioavailability; the use of flutamide with an X_{50}-value of less than 26 µm to increase bioavailability; and use of milling techniques to achieve the specific surface area and/or the X_{50} and/or X_{90} values set forth therein (see column 2, lines 30-35). Given such clear teachings away from the present invention, Applicants respectfully disagree with the Examiner's contention in the sentence spanning pages 13 and 14 of the Office Action that it would be obvious to mix unmilled flutamide in a forced-action mixer with at least one surface-active substance to provide an unmilled flutamide particles having an X50-value greater than 26 µm and a specific surface area of less than 0.35 m^2/cm^3 as presently claimed.

In fact, based on the explicit teaching of James et al. regarding the use of milling to achieve the specific surface area and/or the X_{50} and/or X_{90} values set forth therein (see column 2, lines 30-35), the skilled person would consider milling essential to achieve bioavailability of the "relatively insoluble" flutamide API. As such, there would be no incentive for one skilled in the art to use unmilled flutamide and particle sizes that explicitly fall outside the preferred ranges disclosed in

James et al. This is of particular relevance considering that at the time the present application was filed, the general teaching in the art with regard to low-solubility APIs was that they should be milled or micronized to improve their solubility. See pages 1-3 of the instant specification.

Further, while on the one hand the Examiner asserts that James et al. teach the criticality of the specific surface area and particle size of flutamide particles therein with respect to bioavailability, the Examiner contends on the other hand that "one would be particularly motivated to play with both of these features in order to arrive at a set of flutamide particles with optimal bioavailability." However, such a statement is not supported by the direct teachings of James et al. Indeed, James et al. state:

> "Through significant research, including three series of clinical trials in normal, healthy adult males, a particle size range and range of specific surface area which provide an optimal range of flutamide blood levels in such healthy subjects, in comparison to the innovator product, Eulexin®, has been discovered." See the paragraph spanning columns 1 and 2.

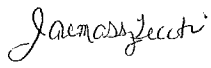
Thus, in so far as James et al. carried out "significant research" to identify "a particle size range and range of specific surface area which provide an optimal range of flutamide blood levels in such healthy subjects," Applicants respectfully submit that the Examiner's rationale of motivation "to play with both of these features in order to arrive at a set of flutamide particles with optimal bioavailability" is flawed. Accordingly, it is respectfully submitted that the claims as currently presented could not be considered obvious in view of the teachings of the primary reference either alone, or in

combination with Neri et al. It is therefore respectfully requested that these rejections under 35 U.S.C. 103(a) be reconsidered and withdrawn.

VI. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



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